Remarks

Claims 1-13 and 16 are pending in the application. Claims 1 and 16 have been amended. Applicant respectfully requests favorable consideration of the amendments and following remarks.

Claim Rejections – 35 U.S.C. §101

Claims 1-12 have been rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. The Examiner contends that in claims 1-12, no transformation is taking place.

Applicants respectfully disagree with the Examiner's contention. Claim 1 recites a computer-implemented method of identifying candidate molecules having a known biological activity or physicochemical property. The method includes the steps of providing a set of field points representing field extrema of a first molecule, wherein each field point has a position and a field size value, the molecule having a known biological activity or physicochemical property; determining at the position of each of the field points of the first molecule the field of a second molecule to obtain a set of field sample values; combining the field sample values with the field size values to provide a score indicative of the field similarity of the first molecule to the second molecule; and providing a measure of the second molecule to have the known biological activity or physicochemical property based on the score.

The claimed process satisfies the "transformation" prong of the "machine-or-transformation" test, and therefore is patent-eligible under §101. Under the transformation prong of the *Bilski* test, data transformations are acceptable if the data represents physical objects or substances (*In re Bilski*, 545 F.3d 943, 962-963, Fed. Cir. 2008). In the claimed process, the data that is transformed represents physical and tangible objects, and their respective structures. Specifically, the field points and field sample values represent information about particular molecules. As stated in the specification at page 4, lines 1-5:

> The field point set encodes a large amount of information about the properties of the molecule, especially regarding its interaction with other molecules. The electrostatic field

> points encode information about the preferred hydrogen-bonding environment of the molecule, while the surface interaction field points encode the molecule's steric bulk.

As illustrated in Fig. 1, the molecular structure and interactions of formic acid are transformed into a set of field points. The field point data is further transformed to a score indicative of the field similarity of a first molecule to a second molecule. The score is used to identify the second molecule as a potential candidate molecule having a known biological or physicochemical activity. The transformation is central to the purpose of the claimed process. Moreover, the claimed process is not an abstract idea, but produces a tangible, real-world result in a form that is useful to the user of the process. Specifically, the claimed process results in the identification of a molecule having a known biological activity or physicochemical property, which is useful to the user of the process in, for example, drug discovery and pharmaceutical research. Process claims 1-12 pass the "machine-or-transformation" test of *Bilski*, and are therefore drawn to patent-eligible subject matter. Applicants respectfully request the reconsideration and withdrawal of the rejection of claims 1-12 under 35 U.S.C. §101.

Claim 16 has been newly rejected under 35 U.S.C. §101, as being directed to non-statutory subject matter. The Examiner contends that an embodiment of the claimed computer apparatus of claim 16 is a program *per se*, and therefore claim 16 is non-statutory.

Claim 16 has been amended to recite a computer apparatus comprising the computer interpretable recording medium of claim 13. In view of the amendment to claim 16, Applicants respectfully request the withdrawal of the rejection of claim 16 under 35 U.S.C. §101.

Claim Rejections – 35 U.S.C. §112

Claims 1-13 and 16 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner contends that it is unclear what applicant intends to claim in the employing step.

Claim 1 has been amended as suggested by the Examiner to recite the step of providing a measure of the second molecule to have the known biological activity or physicochemical property based on the score. In view of the amendment, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112.

Claim Rejections – 35 U.S.C. §103

Claims 1-3, 6, 11-13 and 16 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mestres et al. (J. Molecular Graphics and Modeling, Vol. 15, p. 114-121, 1997) in view of Vinter et al. (IDS ref. 1, filed 11/16/2005) and further in view of Apaya et al. (IDS ref. 2, filed 11/16/2005). It is the Examiner's position that Mestres et al. teaches all of the claim limitations of claim 1, with the exception that Mestres et al. does not show a set of fieldpoints representing field extrema. The Examiner contends that it would have been obvious to modify the method of molecular field comparison of Mestres et al. with the positions and field extrema of Vinter et al. and Apaya et al. because Vintner et al. shows an advantage of comparing field extrema is simplification of the energy map determination, and Apaya et al. shows that by optimizing the overlay of electrostatic extrema it is possible to identify an overlay that has a plausible binding orientation.

Applicants respectfully traverse the rejection for at least the following reasons. As the Examiner himself points out (page 8, lines 15-16 of the Office Action), "Mestres et al. shows that in molecular field similarity comparisons indices can be evaluated for specific points in grid embedding the molecules compared (sic) (page 115, column 2)". Here the Examiner is presumably referring to the first full paragraph in page 115, column 2, which includes equations (2) and (3), where Mestres et al. states that "molecular field-based similarity indices can be evaluated for specific points in a grid embedding the molecules". It is clear from this section of Mestres et al. that what is disclosed is the calculation of these indices at a regular, predefined set of grid points, the calculation of the MFS ("molecular field-based similarity") index being performed as a summation over these grid points (see equation 3).

Hence it is clear that the approach taught in Mestres et al. is quite different than the method of claim 1, which comprises the step of "determining at the position of each

of the field points of the first molecule the field of a second molecule to obtain a set of field sample values".

By contrast, in Mestres et al. there is no suggestion that the similarity metric could be evaluated at locations other than on predefined points of a grid, let alone at arbitrary points determined from the field of one of the molecules. The only step that Mestres et al. suggests beyond the use of regular grid points is that the contributions to the total MFS can be represented "at each of the points on a surface surrounding the superimposed molecules", yet it is clear both from context and from the cited references that what is meant is restricting the extent of the rectilinear grid to cover only part of the molecule.

Furthermore, the Examiner asserts that "'Mestres et al. shows that for each position in the field of the first molecules the field of the second molecule is determined (page 115, column 2)". This is not correct. Mestres et al. shows that for a predetermined set of points in space (with no suggestion that these points can or should be determined with respect to either of the molecules), you can calculate the fields of both molecules and multiply them together. This cannot be equated with "each position in the field of the first molecule", which implies that the positions are somehow chosen with respect to the field of the first molecule.

Also, the Examiner asserts (page 9, lines 1-2) that "Mestres et al. shows the calculation of field size values from an interpolation of a grid (page 117, columns 1-2)". It is unclear which part of page 117 the Examiner is referring to here, since there is no mention of interpolation on this page (or elsewhere in the paper for that matter). Mestres et al. is purely concerned with evaluating fields on grid positions, so has no use for (and does not suggest) interpolation, as there is no need for such a calculation.

The Examiner does however concede that "Mestres et al. does not show a set of field points representing field extrema". This concession is appreciated. Nevertheless, in the light of the above discussion it will be appreciated that this is not the only distinction of the presently claimed method over the Mestres et al. paper, most particularly the fact that Mestres et al. teaches a quite different methodology from that of the present invention as defined by claim 1 which requires the step of "determining at

the position of each of the field points of the first molecule the field of a second molecule to obtain a set of field sample values".

Recognizing (some of) the shortfall of Mestres et al., the Examiner turns to the papers by Vinter et al. and Apaya et al. However, Applicants would submit that not only is the combination of the teachings of Mestres et al. and Vinter / Apaya not the obvious one that the Examiner asserts, but moreover even if one of ordinary skill in the art were to attempt such a combination, there are still claim features that are not disclosed, even by this combination.

The Vinter et al. and Apaya et al. papers are each concerned with taking the field of a molecule, condensing it into a few pharmacophoric points, and then assessing in some fashion the similarity of two such sets of pharmacophoric points. Nowhere in either paper is it mentioned that this is seen as an approximation to a full Mestres-like molecular field similarity integral. The Examiner's contention (page 9. lines 5-7) that "Vinter et al. shows that the field extrema for a (sic) can be compared to the field of another molecule (page 301, column 1)" is not valid.

In Vinter et al., the field of molecule 1 is condensed to a set of field extrema. The field of molecule 2 is likewise condensed to a set of field extrema. All subsequent comparisons are done purely between these sets of extrema. Indeed, Vinter et al. explicitly says "[the] structural features of each pair are no longer relevant in this process" (page 301, column 1), indicating that it is only the two sets of extracted field extrema that are used in the calculation. Comparing two sets of field extrema is not the same as comparing the field extrema for one molecule with the field of another molecule. As such it will be appreciated that Vinter et al. does not disclose "providing a set of field points representing field extrema of a first molecule" and "determining at the position of each of the field points of the first molecule the field of a second molecule to obtain a set of filed sample values".

In fact, Vinter et al. treats the extracted sets of field extrema as sets of point charges in space and evaluates the similarity of the two molecules using the Coulombic attraction between these two sets of point charges (see page 300, "CPF comparisons" and page 301 "Analysis of results"). This similarity measure bears no relation, even conceptually, to the Mestres et al. field similarity integral metric. Equally the approach

in Apaya et al. represents a significantly different approach to the calculation of such a similarity metric, also using two such sets of pharmacophoric points as the starting point and seeking to compare them. There is no suggestion in Apaya et al. to "[determine] at the position of each of the field points of the first molecule the field of a second molecule to obtain a set of field sample points" as required by claim 1.

As a result, the suggested combination of Mestres et al. and Vinter (or Apaya) is far from obvious. The Vinter et al. paper makes no suggestion that it is trying to approximate the full field integral similarity metric, and is explicit in that intermolecular comparisons only use the pre-computed field extrema, with no further reference to the original field of the molecules. The field extrema calculated in Vinter et al. are presented as a simplification of the full molecular field, but comparison of molecules in Vinter et al. only takes place in terms of these simplified representations. Nowhere in either Vinter et al. or Apaya et al. is it suggested that using the full field of one of the molecules rather than its simplified representation would be advantageous.

On the other hand, the Mestres et al. paper is purely concerned with approximating the field integral measure using a rectilinear grid, and makes no suggestion that points "off the grid" could or should be used, or that the points on the grid which are used should be determined with respect to the field of either molecule (as opposed to being predetermined fixed points in space). Hence, the above discussed differences between the present invention as defined in claim 1 and the disclosures of Mestres et al. and Vinter et al. or Apaya et al. notwithstanding, there is no motivation for the skilled person even to consider the proposed combination of these references. Moreover even if one of ordinary skill in the art were to attempt such a combination, there are still claim features that are not disclosed, even by the combination of Mestres et al., Vinter et al. and Apaya et al. Accordingly, prima facie obviousness has not been established and the rejection of claims 1-3, 6, 11-13 and 16 under 35 U.S.C. §103(a) should be withdrawn.

Claims 7-10 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mestres et al. (J. Molecular Graphics and Modeling, Vol. 15, p. 114-121, 1997) in view of Vinter et al. (IDS ref. 1, filed 11/16/2005) and further in view of Apaya et al. (IDS

ref. 2, filed 11/16/2005) as applied to claims 1-3, 6, 11-13 and 16 above, and further in view of Maggiora et al. (Journal of Mathematical Chemistry, Vol. 31, No. 3, April 2002). It is the Examiner's position that Mestres et al. in view of Vinter et al. and in view of Apaya et al. do not show the determination of an aggregate score. The Examiner contends, however, that it would have been obvious to modify the method for comparing the field extrema of a molecule to the field of another molecule to produce a similarity score of Mestres et al. in view of Vinter et al. and in view of Apaya et al. with the determination of an aggregate score of Maggiora et al.

Applicants respectfully traverse the rejection for at least the following reasons. As discussed above, the differences between the present invention as defined in claim 1 and the disclosures of Mestres et al., Vinter et al. and Apaya et al. notwithstanding, there is no motivation for the skilled person even to consider the proposed combination of these references. Moreover even if one of ordinary skill in the art were to attempt such a combination, there are still claim features that are not disclosed, even by the combination of Mestres et al., Vinter et al. and Apaya et al. Maggiora et al. fails to cure the deficiencies of the combination of Mestres et al., Vinter et al. and Apaya et al. Maggiora et al. fails to teach or suggest obtaining a first set of field sample values by determining at the position of each of the field points of the first molecule the field of a second molecule, and then obtaining a second set of field sample values by determining at the position of each of the field points of the second molecule the field of the first molecule. Furthermore, Maggiora et al. fails to teach or suggest providing an aggregate score by combining a first score indicative of the field similarity of the first molecule to the second molecule and a second score indicative of the field similarity of the second molecule to the first molecule. Accordingly, prima facie obviousness has not been established and the rejection of claims 7-10 under 35 U.S.C. §103(a) should be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, request is made for timely issuance of a notice of allowance.

Respectfully submitted,

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/Denise G. Bachtel/ November 3, 2009
Denise G. Bachtel Date